

MULTIVALENT T CELL RECEPTOR COMPLEXES

General Background of the Invention

Field of the Invention

The invention relates to T cell receptors (TCRs) in multivalent form and to their use in detecting cells which carry specific peptide antigens presented in the context of major histocompatibility complex (MHC) at their surface. The invention further relates to delivery methods, in particular for the delivery of therapeutic agents, to target cells using the multimeric TCRs.

Description of the Related Art

1. Antigen presentation on the cell surface

MHC molecules are specialised protein complexes which present short protein fragments, peptide antigens, for recognition on the cell surface by the cellular arm of the adaptive immune system.

Class I MHC is a dimeric protein complex consisting of a variable heavy chain and a constant light chain, β_2 microglobulin. Class I MHC presents peptides which are processed intracellularly, loaded into a binding cleft in the MHC, and transported to the cell surface where the complex is anchored in the membrane by the MHC heavy chain. Peptides are usually 8-11 amino acids in length, depending on the degree of arching introduced in the peptide when bound in the MHC. The binding cleft which is formed by the membrane distal α_1 and α_2 domains of the MHC heavy chain has "closed" ends, imposing quite tight restrictions on the length of peptide which can be bound.

Class II MHC is also a dimeric protein consisting of an α (heavy) and β (light) chain, both of which are variable glycoproteins and are anchored in the cell by transmembrane domains. Like Class I MHC, the Class II molecule forms a binding cleft in which longer peptides of 12-24 amino acids are inserted.

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